REMARKS

Claims 1-8 are pending in the above-identified application and stand ready for further action on the merits.

Interview with Examiner

Applicants appreciate the Examiner's courtesy in holding a personal interview on January 14, 2004 with Applicants' representative, John W. Bailey. The Examiner's statement in the Interview Summary correctly sets forth the subject matter discussed in the interview. It is also noted that the present response is in line with discussions held during said interview. It is hoped that the present response will result in an allowance of each of the pending claims 1-8.

Claim Rejections Under 35 USC § 103

Claims 1-8 have been rejected under 35 USC § 103(a) as being unpatentable over Fujioka et al. US '547 (US 5,851,547) in combination with Hudson et al. EP '410 (EP 0009410 A2).

The Present Invention and Its Advantages

The present invention provides for controlled release preparations having multi-layer structures. The preparations more particularly relate to controlled drug-release formulations having

multi-layer structures, wherein one or more drugs can separately be released with a different behavior in vivo, for the purpose of effectively exhibiting the efficacy thereof.

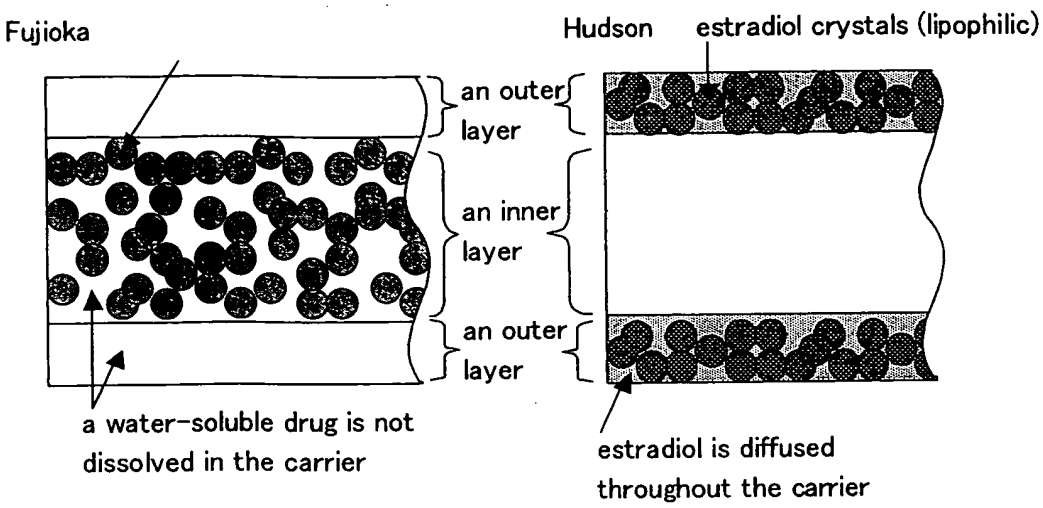
In the present specification, experiments are carried out and reported between preparations of the present invention and comparative preparations. As seen upon reviewing experiments 1-4 at pages 20-21 of the specification, and Figures 2-5 referred to therein, the Examiner can easily see that the compositions of the present invention possess advantageous properties, and allow one to easily release one or more drugs separately with different behaviors in vivo.

Distinctions over the Cited Art

Non-obviousness of the Invention over the Combination of References

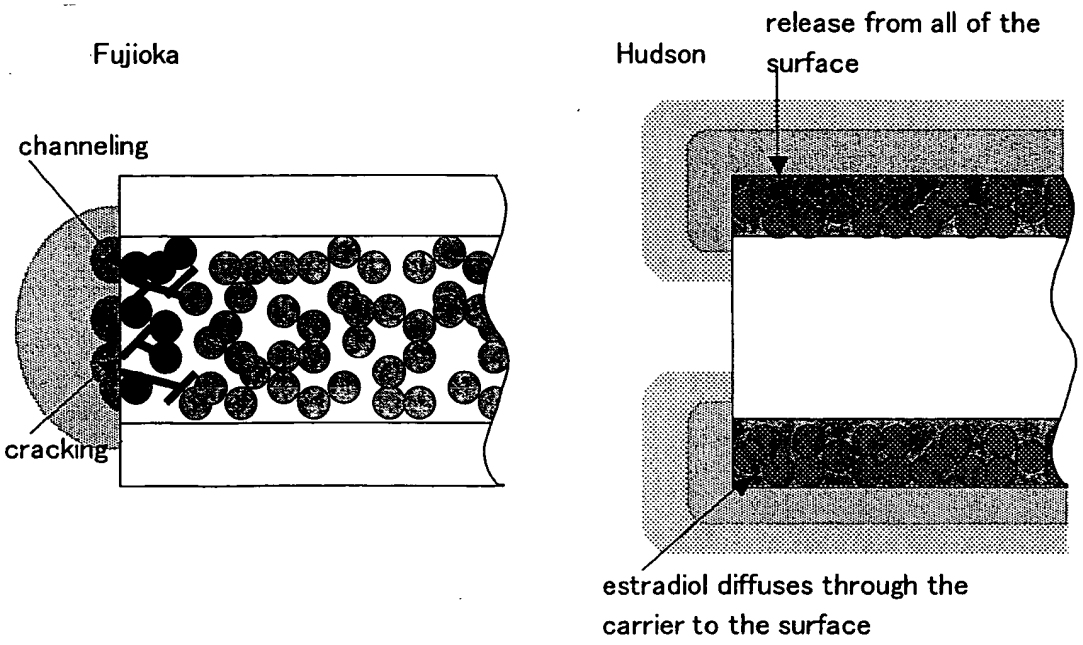
The structure of the formulation disclosed in Fujioka and Hudson are as schematically shown below, respectively. Hudson teaches a cylindrical implantable formulation comprising estradiol as a drug. However, estradiol is not a water-soluble drug but a lipophilic drug. Accordingly, the combination of Fujioka and Hudson might motivate one skilled in the art to prepare an implantable preparation wherein a lipophilic drug is comprised in the outermost layer. However, the preparation as instantly claimed

wherein the outermost layer comprises a water-soluble drug was not obvious at the time the invention was made.



A crosssectional view before implantation

Furthermore, Fujioka teaches that a channeling phenomenon participates in the release process for water-soluble drugs from hydrophobic polymer carriers. Here, the drug present in the vicinity of the surface of the formulation first dissolves in the ambient water (see col. 1, lines 47-56 of Fujioka; and also see page 59, right column, lines 13-31 of Journal of Controlled Release 66 (2000), 49-61). Thus, long-term zero-order release of the water-soluble drug from the formulation of Fujioka is achieved by such process as schematically shown below. On the other hand, in the preparation of Hudson, estradiol diffuses through dimethylpolysiloxane silicone rubber to the surface where it is released into the animal tissue, as schematically shown below (see page 4, lines 1-4 of Hudson).



A crosssectional view after implantation

Thus, when estradiol is used in the formulation of Fujioka, one of ordinary skill in the art would anticipate that estradiol diffuses through dimethylpolysiloxane rubber, such as Dow Corning® MDX 4-4210, to the surface, whichever it is comprised in an inner layer or the outermost layer. Such diffusion of estradiol through dimethylpolysiloxane rubber would not provide zero-order release since estradiol released from the formulation was decreased over time, as shown in the table disclosed in Hudson (page 8). Therefore, the teaching of Hudson would not motivate one of ordinary skill in the art to apply estradiol to the formulation of Fujioka, in order to provide a multiple drug delivery system that achieves a zero-order release profile over an extended period of time.

CONCLUSION

Accordingly, based upon the above considerations, the Examiner is respectfully requested to reconsider the outstanding rejection under 35 USC § 103 and to issue a Notice of Allowance clearly indicating the patentability of each of pending claims 1-8.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact John W. Bailey (Reg. No. 32,881) at the telephone number below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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